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CHEMICAL CONSTITUTION AND ACTIVITY OF BIPYRIDYLIUM HERBICIDES—II*

DIQUATERNARY SALTS OF 1,10-PHENANTHROLINE

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Abstract—1,10-Phenanthroline reacts with ethylene dibromide and 1,3-dibromopropane to give the bridged diquaternary salts 5,6-dihydropyrazino[1.2.3.4-*lmn*]1,10-phenanthrolinium dibromide and 5*H*-6,7-dihydro-1,4-diazepino[1.2.3.4-*lmn*]1,10-phenanthrolinium dibromide respectively. The salts are rapidly reduced in aqueous solution by a one electron transfer to give stable radical cations which to a large extent are oxidised back to the diquaternary salts by air. The phenanthroline salts are phytotoxic but they are not as active as bipyridylium herbicides. Possible reasons for this are discussed.

DIQUAT (I), paraquat (II) and related diquaternary salts of 2,2'- and 4,4'-bipyridyls have attracted much attention as herbicides.[1] Their mode of action is thought[2–4] to be connected with their ability to be rapidly reduced in aqueous solution to stable radical cations at a potential (E_0) of about $-0{\cdot}35$ to $-0{\cdot}45$ volts by a one electron transfer which is rapidly and quantitatively reversed by oxygen. The stability of the radical cations is due to the delocalization of the odd electron over both pyridine rings which are essentially co-planar. Certain diquaternary salts of phenanthrolines might be expected to behave similarly but only salts of 4,7- and 1,8-phenanthrolines have so far been investigated as herbicides and these were found[2] to give unstable radicals on reduction and to be inactive as herbicides. The choice of 4,7- and 1,8-phenanthrolines for examination as herbicides, however, does not seem appropriate since these isomers are analogues of 3,3'- and 2,4'-bipyridyls respectively and diquaternary salts of these bipyridyls are either inactive or are mediocre herbicides.[2] It is more pertinent to investigate diquaternary salts of 1,10- and 3,8-phenanthrolines where the nitrogen atoms are in the same relative positions as in 2,2'- and 4,4'-bipyridyls. This paper describes the preparation and some of the properties of diquaternary salts of 1,10-phenanthroline. Parts of the work have been reported in preliminary communications[5,6] and in a lecture report.[7]

Because of steric difficulties it has not been found possible to obtain diquaternary salts of 1,10-phenanthroline from simple alkyl halides.[8] Ethylene dibromide, however, reacts with 2,2'-bipyridyl[9] to give diquat (I) and with 2,2'-dipyridyl sulphide[10,11] to afford the bridged diquaternary salt III. 1,10-Phenanthroline reacted similarly with ethylene dibromide to give the cyclic salt 5,6-dihydropyrazino[1.2.3.4-*lmn*]-1,10-phenanthrolinium dibromide (IV), the structure of which was confirmed by elemental analyses (all bromine ionic) and by the NMR spectrum. With 1,3-dibromopropane, 1,10-phenanthroline likewise afforded 5*H*-6,7-dihydro-1,4-diazepino[1.2.3.4-*lmn*]1,10-phenanthrolinium dibromide (V). As expected for derivatives of the

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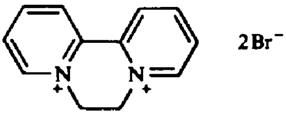
* Part I, L. A. Summers, *Tetrahedron*, **24**, 2697 (1968).

rigid planar phenanthroline ring system the UV spectra of IV and V were almost identical (cf. Ref. 2). The solid diquaternary salts of 1,10-phenanthroline tended to be hygroscopic. They were stable in aqueous solution and, as expected, were decomposed by alkali.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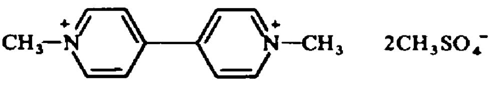
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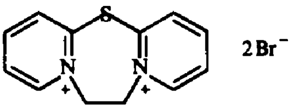
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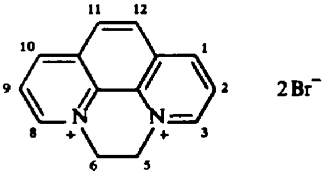
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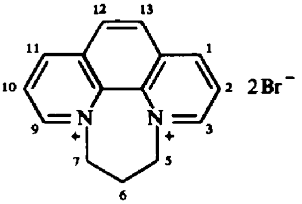
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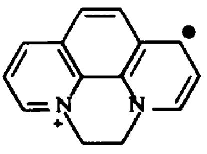
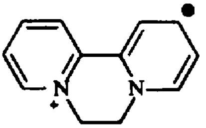

VI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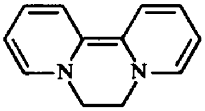
VIII

Aqueous solutions of IV and V on treatment with zinc dust immediately developed an intense deep red colouration which is attributed to the corresponding radical cation. Structure VI, for example, is one of the many canonical forms of the radical cation from compound IV. The presence of a high concentration of a stable radical was confirmed in each case by examination of the NMR spectrum of the intensely coloured solution. The signals due to the aromatic protons in *meta* and *para* positions to the quaternary N atoms in IV and V had disappeared. Those from the other aromatic protons were still present, but they had degenerated considerably. These findings clearly indicate that a paramagnetic species is present and suggest that the odd electron is not uniformly delocalized over the three aromatic rings. The signals due to the methylene groups adjacent to the quaternary N atoms had lost much of their resolution but those from the central methylene protons of V remained relatively unaffected. When the reducing agent was removed and the solution was shaken for about 15 seconds in air the deep colour substantially discharged. The NMR spectrum obtained then was essentially that of the original diquaternary salt although there were clearly small amounts (~ 10%) of unidentified by-products present.

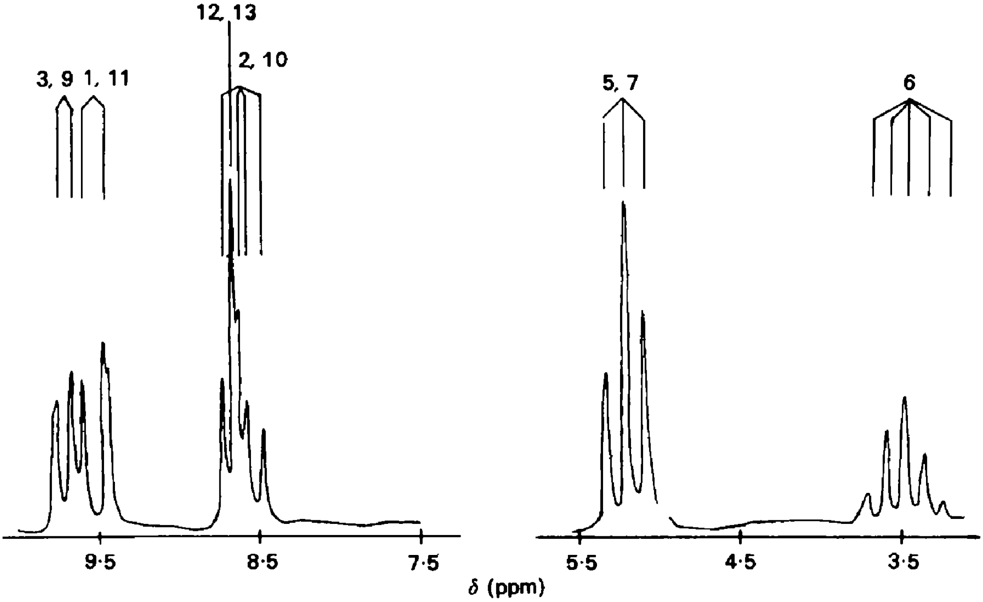

FIG. 1 NMR spectrum in D_2O of 5*H*-6,7-Dihydro-1,4-diazepino[1.2.3.4-*lmn*]1,10-phenanthrolinium dibromide (V). D_2O signal is omitted.

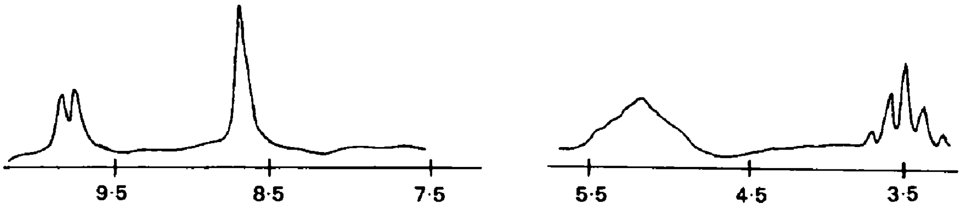

FIG. 2 NMR spectrum in D_2O of radical cation obtained from V by treatment with zinc dust.

Results obtained from polarography were consistent with the uptake of one electron by the diquaternary salts. At concentrations of 0·001 M and 0·0015 M in the pH range 6–8 the phenanthroline diquaternary salts each gave typical symmetrical one electron reduction waves with half-wave potentials (E_0) of about −0·27 volts independent of pH and concentration. A second reduction wave was also present ($E_0 \sim -0{\cdot}85$ volts) but it was not clear-cut and was not investigated further. Diquat dibromide (I) was included in the polarograph experiments for comparison and gave as before,[12] two distinct reduction waves with E_0 values of $-0{\cdot}36$ and about $-0{\cdot}75$ volts due to the formation of VII and presumably VIII respectively.

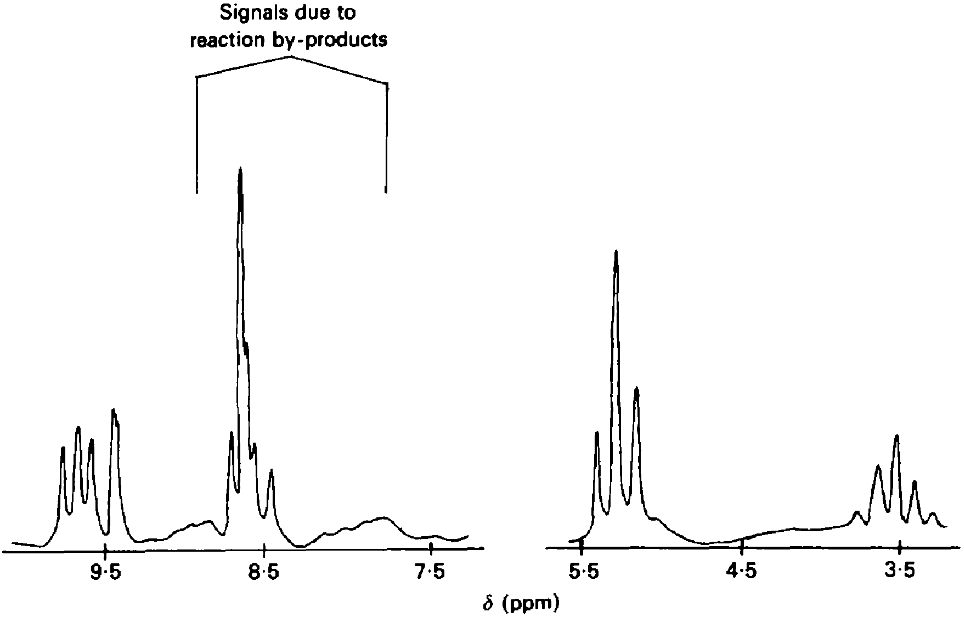

FIG. 3 NMR spectrum in D_2O obtained by atmospheric oxidation of the radical cation of V.

It is apparent from these results that the diquaternary salts of 1,10-phenanthroline are rapidly reduced in aqueous solution to stable radical cations at a higher potential than diquat and that the one electron transfer is largely, but not quantitatively, reversed by atmospheric oxidation.

In herbicidal tests the diquaternary salts of 1,10-phenanthroline at a high concentration desiccated green plant tissue in a manner typical of bipyridylium herbicides although at practical rates of application equivalent to 4 lbs and 8 lbs/acre on six plant species[6] they were clearly much inferior to diquat. The discovery of herbicidal activity, although of a relatively low order, in diquaternary salts of 1,10-phenanthroline demonstrates that the phytotoxic action of the diquat and paraquat type is not confined to diquaternary salts of bipyridyls as has been supposed.[2] It also strongly supports the view that the herbicidal action of the bipyridyls is associated with their reversible one electron transfer properties.[1,2,3,4,13] The reasons for the relatively low activity of the diquaternary salts of 1,10-phenanthroline are probably connected with their relatively large values of E_0 which presumably lie just outside the potential range of the biochemical electron transfer processes with which the bipyridylium herbicides are thought to interfere. However, other factors may also be involved. 1,10-Phenanthroline is a larger molecule than 2,2'- and 4,4'-bipyridyls and it may be that its diquaternary salts find difficulty in reaching the site of biological action because of their size. This suggestion recalls that certain diquaternary salts of 4,4'-bipyridyl containing long alkyl quaternising groups[1,2] and diquaternary salts of phenyl substituted 4,4′-bipyridyls[14] are inactive as herbicides although they meet other requirements thought to be necessary for herbicidal activity.[2] Moreover, the fact that the one electron transfer between the phenanthroline diquaternary salts and their respective radical cations is not quite quantitatively reversible may also have some bearing on their reduced level of activity since continual regeneration of the diquaternary salts from their radical cations is currently thought[1, 2, 4, 13] to be an important step in the phytotoxic process with bipyridylium herbicides. It is hoped that some of these points will be clarified as a result of work with related systems at present being investigated.

EXPERIMENTAL

UV absorption spectra were taken with 0·0001 M solns in water. NMR spectra were determined at 60 Mc/s using sodium 3-trimethylsilyl-1-propane sulphonate as internal standard. Polarograph experiments were carried out on 0·001 M and 0·0015 M aqueous solns at 20° in 0·067 M Sorensen phosphate buffers at pH 5·9, 6·8 and 8·04 using a standard calomel electrode. The half-wave potentials are assumed to be E_0 values and were calculated by adding 0·25 volts to the $E_{\frac{1}{2}}$ values. Experimental error is ±0·02 volts. Microanalyses were by the Australian Microanalytical Service.

5,6-*Dihydropyrazino*[1.2.3.4- 1mn]1,10-*phenanthrolinium dibromide* (IV) was prepared by treating 1,10-phenanthroline hydrate with boiling ethylene dibromide for 45 min. The ppt which was obtained was crystallized from aqueous EtOH to give the product as brownish crystals, m.p. >390°; yield = 70% UV spectrum λ_{max} 226 (log ε 4·32), 279 (4·61), 295 (3·81), 308 (3·87), 318 mμ (3·78); NMR spectrum (D_2O) δ5·8 (4H, s, methylene), 8·6–8·9 (2H, m, 2,9 aromatic), 8·85 (2H, s, 11,12 aromatic), 9·55–9·8 ppm (4H, t. 1,3,8,10 aromatic). Reduction potential E_0 −0·28 volts. (Found: C, 45·4; H, 3·4; N, 7·5; Br (ionic) 43·3 $C_{14}H_{12}Br_2N_2$ requires: C, 45·65; H, 3·3; N, 7·6; Br (ionic) 43·5%).

5H-6,7-*Dihydro*-1,4-*diazepino*[1.2.3.4-1mn]1,10-*phenanthrolinium dibromide* (V) was prepared similarly using 1,3-dibromopropane (30 min). It crystallized from aqueous EtOH to give the product as pale yellow crystals, m.p. 286° (with dec); yield = 80%; UV spectrum λ_{max} 226 sh (log ε 4·32), 281 (4·59), 298 (3·76), 311 (3·83), 322 sh mμ (3·70). Figures 1, 2 and 3 show the NMR spectrum (D_2O) δ3·25–3·7 (2H, m, 6 methylene), 5·1–5·3 (4H, t, 5,7 methylene), 8·5–8·75 (2H, m, 2,10 aromatic), 8·65 (2H, s, 12,13 aromatic), 9·4–9·6 (2H, d, 1,11 aromatic), 9·65–9·8 ppm (2H, d, 3,9 aromatic). Reduction potential E_0 −0·27 volts. (Found: C, 47·1; H, 3·8; N, 7·1; Br (ionic) 41·7. $C_{15}H_{14}Br_2N_2$ requires: C, 47·1; H, 3·7; N, 7·3; Br (ionic) 41·9%).

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